Conversion of human fibroblasts into functional cardiomyocytes by small molecules.

Journal: Science

Publication Year: 2016

Authors: Nan Cao, Yu Huang, Jiashun Zheng, C Ian Spencer, Yu Zhang, Ji-Dong Fu, Baoming Nie, Min Xie, Mingliang Zhang, Haixia Wang, Tianhua Ma, Tao Xu, Guilai Shi, Deepak Srivastava, Sheng Ding

PubMed link: 27127239

Funding Grants: A new paradigm of lineage-specific reprogramming

Public Summary:
Reprogramming somatic fibroblasts into alternative lineages would provide a promising source of cells for regenerative therapy. However, transdifferentiating human cells into specific homogeneous, functional cell types is challenging. Here we show that cardiomyocyte-like cells can be generated by treating human fibroblasts with a combination of nine compounds that we term 9C. The chemically induced cardiomyocyte-like cells uniformly contracted and resembled human cardiomyocytes in their transcriptome, epigenetic, and electrophysiological properties. 9C treatment of human fibroblasts resulted in a more open-chromatin conformation at key heart developmental genes, enabling their promoters and enhancers to bind effectors of major cardiogenic signals. When transplanted into infarcted mouse hearts, 9C-treated fibroblasts were efficiently converted to chemically induced cardiomyocyte-like cells. This pharmacological approach to lineage-specific reprogramming may have many important therapeutic implications after further optimization to generate mature cardiac cells.

Scientific Abstract:
Reprogramming somatic fibroblasts into alternative lineages would provide a promising source of cells for regenerative therapy. However, transdifferentiating human cells into specific homogeneous, functional cell types is challenging. Here we show that cardiomyocyte-like cells can be generated by treating human fibroblasts with a combination of nine compounds that we term 9C. The chemically induced cardiomyocyte-like cells uniformly contracted and resembled human cardiomyocytes in their transcriptome, epigenetic, and electrophysiological properties. 9C treatment of human fibroblasts resulted in a more open-chromatin conformation at key heart developmental genes, enabling their promoters and enhancers to bind effectors of major cardiogenic signals. When transplanted into infarcted mouse hearts, 9C-treated fibroblasts were efficiently converted to chemically induced cardiomyocyte-like cells. This pharmacological approach to lineage-specific reprogramming may have many important therapeutic implications after further optimization to generate mature cardiac cells.